Claim 79

Applicants had requested rejoinder of claim 79 to examined claims 16-78. The Examiner quoted

> [n]ucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 *et seq.*

M.P.E.P. § 803.04.

The Examiner ignored the rest of the paragraph from which the above quote originated. The remaining part of the paragraph states

> [n]evertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR 1.141 *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application.

M.P.E.P. § 803.04. Further, "normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction." *Id.*

Thus, while it is true that nucleotide sequence encoding different proteins are independent and distinct and *ordinarily* would be subject to a restriction requirement, up to ten nucleotide sequences encoding different proteins should be examined together in one application. Thus, in the present case, the invention of claim 79 should be examined along with the invention of claims 16-78.

Rejection of claims 16-78 under 35 U.S.C. § 101/ 35 U.S.C. § 112

The Examiner rejected claims 16-78 under 35 U.S.C. § 101 as allegedly lacking utility. Applicants respectfully traverse this rejection.

The Examiner states that

> [t]he specification discloses SEQ ID NO:1, the polynucleotide sequence of BCSG1, an mRNA, which when used as a hybridization probe can distinguish metastatic breast cancer tissue from normal breast tissue (p.48 of the specification). Thus, the polynucleotide sequence of SEQ ID NO:1 has utility as a probe for the detection of metastatic breast cancer. However, while it is noted that the polypeptide encoded by SEQ ID NO:1 has 54% sequence identity to the human Alzheimer's disease amyloid protein (see p. 46, lines 24-25), the function of this polypeptide (amino acid sequence of SEQ ID NO:2, encoded by SEQ ID NO:1) is not known. Thus, polynucleotide sequences that encode the polypeptide of SEQ ID NO:2, or fragments thereof lack a specific, substantial and credible utility.

Paper No. 15, § 5.

To satisfy the requirements of 35 U.S.C. § 101, Applicants "must show that the claimed invention is 'useful' for some purpose either explicitly or implicitly." M.P.E.P. § 2107 at 2100-30. Furthermore, Applicants need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. § 101 and 35 U.S.C. § 112. *See, e.g., Raytheon v. Roper*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835 (1984).

Applicants assert that the invention satisfies the utility requirement. As the Examiner noted, polynucleotides having the nucleotide sequence of SEQ ID NO:1 are useful for distinguishing cancerous breast tissue from normal breast tissue. Polynucleotides comprising SEQ ID NO:1 or portions thereof are recited in claims 17, 19 and 43. Claims 44-56 depend from

claim 43. Thus, by the Examiner's own admission, claims 17, 19 and 43-56 satisfy the utility requirement.

Polynucleotides of the invention are useful as a hybridization probe for detecting expression in specific tissues, regardless of whether or not they encode a polypeptide or are completely identical to SEQ ID NO:1. *See* specification, page 12, line 23 to page 13, line 7. Further, page 25, line 17 to page 29, line 28, provides both specific instances where detection of BCSG1 would be desirable, and methods of detecting BSCG1 expression using nucleotide probes or antibodies. For example, as the Examiner noted, detection of BSCG1 expression is useful to detect metastatic breast cancer tissue.

The polynucleotides of the invention, besides being useful themselves as breast cancer probes, are useful for producing polypeptides which raise antibodies for detecting metastatic breast cancer. Page 24, lines 22-27 describes the regions of the BCSG1 polypeptide which may be used to generate BCSG1 specific antibodies. Page 29, lines 16-24 describe antibody-based methods for assaying BCSG1 protein levels.

Applicants assert that the use of the polynucleotides to detect metastatic breast cancer tissue, or to produce polypeptides to raise antibodies to detect metastatic breast cancer tissue, is specific, substantial and credible. Not every polynucleotide may be used to detect breast cancer tissue; thus, this use is specific. This use is substantial, "real world" use as the polynucleotides may be used to detect an identified disease, *i.e.*, breast cancer. Finally, the use is credible, as it is demonstrated in Example 6 that BSCG1 is expressed in cancerous, but not benign, breast tissue. Applicants assert that the uses of the polynucleotides to detect metastatic breast cancer or to produce polypeptides to raise antibodies to detect metastatic breast cancer are sufficient to fulfill the requirements of 35 U.S.C. § 101. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 101 be reconsidered and withdrawn.

The Examiner has also rejected claims 16-78 under 35 U.S.C. § 112, first paragraph. For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. § 101 rejection is proper." M.P.E.P. § 2107(IV) at 2100-28 (Rev.1, Feb. 2000). Therefore, since the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejection of claims under 35 U.S.C. § 112, first paragraph, based on lack of utility of the claimed invention, should be withdrawn.

Rejection of claims 17, 19 and 77 under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 17, 19 and 77 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Applicants respectfully traverse this rejection.

The Examiner states

> [t]he applicants broadly contemplated a genus of polynucleotides, those encoding the BCSG1 polypeptide having the amino acid sequence in Figure 1 (SEQ ID NO:2) and those encoding the polypeptide having the amino acid sequence of SEQ ID NO:2, but lacking the N-terminal methionine. No where in the specification is there support for the species of molecule which is nucleotide 15 to 392 of SEQ ID NO:1 or nucleotide 12 to 392 of SEQ ID NO:1, that is there is no evidence that, at the time of filing, the claimed nucleotides started specifically at residue 12 or residue 15 of SEQ ID NO:1.

Paper No. 15, § 3.

The Examiner is reminded that the adequate written description requirement serves to ensure that the inventor had possession, as of the filing date, of the claimed subject matter.

However, "how the specification accomplishes this is not material." *In re Wertheim*, 191 U.S.P.Q. 90, 96 (C.C.P.A. 1976). Further, "[i]f a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met." *In re Alton*, 37 U.S.P.Q. 2d 1578, 1584 (C.A.F.C. 1996).

The Federal Circuit recently reaffirmed that *ispis verbis* description of an invention is *not* required by § 112, first paragraph. *Union Oil Co. of California v. Atlantic Richfield Co.*, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000) ("*Unocal*"). Instead, when the skilled person could discern that the claimed invention was in the possession of the applicants upon reading the specification, then the written description requirement has been met. *See Unocal*. Thus, in the present situation, the standard for adequate written descriptive support is not whether the numbers "12 to 392" or "15 to 392" appear in the specification, but instead whether a person of ordinary skill would have understood, from reading the specification, the present inventors to have been in possession of the claimed subject matter, *i.e.*, a polynucleotide comprising nucleotides 12 to 392 or 15 to 392 of SEQ ID NO:1.

In the sequence listing, which is part of the application as filed, under item (ix) of SEQ ID NO:1, lists the location of the codons as 12 to 392. Additionally, the nucleotides of SEQ ID NO:1 are numbered, and the corresponding amino acid sequence of SEQ ID NO:2 is shown underneath the nucleotides of SEQ ID NO:1. The amino acids of SEQ ID NO:2 shown under the nucleotides of SEQ ID NO:1 are also numbered. Thus, the sequence listing depicts that nucleotides 12 to 392 of SEQ ID NO:1 encode amino acids 1 to 127 of SEQ ID NO:2 and nucleotides 15 to 392 of SEQ ID NO:1 encode amino acids 2 to 127 of SEQ ID NO:2. Similarly,

Figure 1 shows that nucleotides 12 to 392 and 15 to 392 of SEQ ID NO:1 encode amino acids 1 to 127 and 2 to 127 of SEQ ID NO:2, respectively.

Moreover, at page 6, lines 26-29 of the specification states that SEQ ID NO:1 encodes "a protein of 127 amino acid residues, with an initiation codon at positions 12-14 of the nucleotide sequence in Figure 1 (SEQ ID NO:1)". Thus, the specification explicitly states that the starting nucleotide in SEQ ID NO:1 for encoding the amino acid sequence of SEQ ID NO:2 is at position 12 and implicitly states that the starting nucleotide in SEQ ID NO:1 for the second amino acid of SEQ ID NO:2 is at position 15.

Applicants submit that from the extensive written description of the claimed invention in the sequence listing, specification and drawings, one of ordinary skill in the art would understand that the inventors were in possession of a polynucleotide comprising nucleotides 12 to 392 or 15 to 392 of SEQ ID NO:1. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection of claims 43-70 and 78 under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 43-70 and 78 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. Applicants respectfully traverse this rejection.

The Examiner states that

> the genus of nucleic acid molecules comprising only a partial sequence encompasses a variety of subgenera with widely varying attributes. The specification discloses only the structural features of one species, the polynucleotide sequence of SEQ ID NO:1. The specification lacks information to lead one of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed.

Paper No. 15, § 6. Each of the species falling within the claims possesses the common attributes of being useful for detecting metastatic breast cancer and of comprising a portion of SEQ ID

NO:1 or encoding a portion of SEQ ID NO:2. As discussed below, Applicants have disclosed a number of species besides SEQ ID NO:1.

The Examiner directed Applicants' attention to the Revised Interim Written Description Guidelines Training Materials. The Examiner appears to be relying on Example 7 of the Training Materials in making this rejection. In Example 7 of the Training Materials, an isolated cDNA comprising "SEQ ID NO:16" is claimed. In reference to the hypothetical application, the Training Materials state

> a partial cDNA sequence that is claimed with open language (comprising), the genus of, e.g., "A cDNA comprising [a partial sequence]," encompasses a variety of subgenera with widely varying attributes. For example, a cDNA's principle attribute would include its coding region. A partial cDNA that did not include a disclosure of any open reading frame (ORF) of which it would be a part, would not be representative of the genus of cDNAs because no information regarding the coding capacity of any cDNA molecule would be disclosed.

Revised Interim Written Description Guidelines Training Materials, page 31. The implication in this passage is that if the entire ORF is disclosed, then this disclosure is representative of the genus of polynucleotides.

In the present case, and in contrast to Example 7 of the Training Materials, Applicants have disclosed the entire ORF. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Regents of the University of California v. Eli Lilly & Co.*, 43 U.S.P.Q. 2d 1398 (Fed. Cir. 1997), *cert. denied*, 66 U.S.L.W. 3688 (1998). Applicants assert that the disclosure of the entire ORF is representative of the genus of polynucleotides encompassed by the claims.

Nevertheless, Applicants have disclosed more than one single species. For example, with respect to claims 43 and 78, Applicants have not only disclosed the full length polynucleotides, but also fragments of SEQ ID NO:1 which are 50, 75, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, 500, 525 and 550 nucleotides in length. Each of these fragments are species falling within the claimed genus. With respect to claim 57, Applicants have described both full length SEQ ID NO:1 and the particular fragments themselves, both of which are species falling within the genus of the claims.

Additionally, one of skill in the art can readily envisage nucleic acid sequences which include fragments of SEQ ID NO:1 or encoding fragments of SEQ ID NO:2, because, for example, SEQ ID NO:1 can be readily embedded in known vectors. Although there may be substantial variability among the species of polynucleotides encompassed within the scope of claims 43 and 57, because the fragments may be combined with sequences known in the art, the necessary common attribute is the fragment of SEQ ID NO:1 or encoding SEQ ID NO:2. Thus, the disclosure of the several species described above is sufficient to fulfill the written description requirement.

Further, claim 78 recites polynucleotides which hybridize under stringent conditions. A person of ordinary skill in the art would not expect substantial variation among species encompassed within the scope of claim 78 because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, since there is little variability among the species of the claim 78, the description of the several species described above is sufficient to fulfill the written description requirement.

Applicants submit that all of the claims meet the written description requirement. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Andrea Jo Kamage

Andrea Jo Kamage
Agent for Applicants
Registration No. 43,703

Date: August 6, 2000

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

P98-30.wpd